correlated with BP, and in silico findings were validated by immunohistochemistry of kidney tissues. RESULTS/ANTICIPATED RESULTS: On the LS diet, Na+ intake and serum 17 beta-estradiol concentration correlated with BP. Cell type composition of renal biopsies was consistent among all animals for both diets. Kidney transcriptomes differed by diet; analysis by unbiased weighted gene co-expression network analysis revealed modules of genes correlated with BP on the HS diet. Network analysis of module genes showed causal networks linking hormone receptors, proliferation and differentiation, methylation, hypoxia, insulin and lipid regulation, and inflammation as regulators underlying variation in BP on the HS diet. Our results show variation in BP correlated with novel kidney gene networks with master regulators PPARG and MYC in female baboons on a HS diet. DISCUSSION/SIGNIFICANCE: Previous studies in primates to identify molecular networks dysregulated by HS diet focused on males. Current clinical guidelines do not offer sex-specific treatment plans for sodium sensitive hypertension. This study leveraged variation in BP as a first step to identify correlated kidney regulatory gene networks in female primates after a HS diet.

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Integrated Analysis of Genetic Databases Identifies miRNA Associated With Poor Survival In Melanoma

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OBJECTIVES/GOALS: Despite advances in precision medicine and understanding of the molecular pathways, melanoma remains the deadliest skin cancer, warranting identification of novel biomarkers. In this study, we performed bioinformatic analysis of melanoma patient tumors to identify novel dysregulated gene and micro-RNA (miRNA) targets responsible for survival. METHODS/STUDY POPULATION: Genetic sequencing data for 594 patient samples of melanoma and normal skin tissue from 10 databases were accessed using the NCBI Gene Expression Omnibus. Genes and miRNA that were significantly dysregulated (adjusted p-value < 0.05, log fold change > Â± 2) in melanoma compared to normal skin were identified using the GEO2R program. Dataset expression profiles were cross-referenced to identify genetic elements dysregulated in at least 50% of datasets and filtered for association with poor survival using R2 Genomics Analysis and Visualization Platform. DAVID 6.8 provided pathway analysis of dysregulated genes. miRTarBase linked genes associated with poor survival and dysregulated miRNA from our database analysis. RESULTS/ANTICIPATED RESULTS: Bioinformatic analysis revealed consistent differential regulation of 205 genes (down=177 and up=28) and 38 miRNA across datasets with fold change >2 (bonf. p<0.05). Pathway analysis indicated that PPAR, phosphatidylinositol signaling, Rap1 signaling, and p53 signaling pathways were enriched by downregulated genes while the NF-kB pathway was enriched up regulated genes. Survival analysis of the differentially regulated genes identified 11 downregulated (ACSL1, CEBPA, CES4A, CRIP1, GATA3, HLADQB2, PTGS1, PYCARD, PPARG, PKP3, RSSF6) and 3 upregulated (DUXAP10, SLC2A3 and PRAME) hub genes to be associated with poor overall survival. Out of the 13 miRNA associated with hub genes, five miRNA (hsa-miR-125b-5p, hsa-miR-130b-3p, hsa-miR-26n-5p, hsa-miR-30b, hsa-miR-30c) were linked to multiple hub genes. DISCUSSION/SIGNIFICANCE: Our analysis identified 14 hub genes (regulators of PPARA, adipocyte differentiation, and transcriptional pathways) as well as miRNAs hsa-miR-30c (regulator of PTGS1 and SLC2A3) and hsa-let-7i-5p (regulator of ASCL1) as potential therapeutic targets. Further studies for validation of the targets are needed for clinical translation in melanoma.

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Nociplastic pain and early discontinuation of aromatase inhibitor therapy in breast cancer patients over age 65*

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OBJECTIVES/GOALS: Side effects are why up to 50% of women with hormone-positive breast cancer prematurely discontinue aromatase inhibitor (AI) therapy. Pain from altered nociception without clear tissue/nerve damage (nociplastic) is a hypothesized contributing factor to this. Our objective was to evaluate the relationship between nociplastic pain and AI duration. METHODS/STUDY POPULATION: Patients with breast cancer diagnosed between 2012-19 were identified from the University of Michigan Genomics Initiative (MGI). Patients who were female, >65 years old at time of breast cancer diagnosis, and had hormone receptor-positive disease met inclusion criteria. Prior to undergoing surgery, patients completed validated surveys about overall worst pain (Brief Pain Inventory [BPI]), nociplastic pain (2011 Fibromyalgia Survey [FS]), and life satisfaction, with higher scores representing more of the factor. Breast cancer history, treatment, and patient demographics were abstracted from the medical record. Univariate analysis was conducted to evaluate the relationship between age, body-mass index (BMI), chemotherapy, BPI, FS, life satisfaction, and time to discontinuation of initial AI. RESULTS/ANTICIPATED RESULTS: 207 patients were eligible, 133 of whom initiated AI therapy. Of the 133 analyzed patients, mean age was 70.7 years and mean BMI was 30.3. 28 (21%) underwent adjuvant chemotherapy and 79 (59%) received adjuvant radiation prior to initiation of AI therapy. Average nociplastic pain score was 4.0/31 (standard deviation [SD] 4.6), worst pain was 1.5/10 (SD 1.9), and life satisfaction score was 7.3/10 (SD 2.8). The initial AI for 94% of patients (125 patients) was anastrozole. On univariate analysis, only higher nociplastic pain score was statistically associated with premature discontinuation of AI with a HR 1.07 (95%CI 1.00-1.13, p = 0.036). On multivariable analysis, no factors remained statistically significant, although there was a trend for nociplastic pain (HR 1.06, 95%CI 1.00-1.13, p = 0.068). DISCUSSION/SIGNIFICANCE: It is important to identify variables predicting tolerance to therapy so patients can be optimally counseled. Our study suggests that patients with pre-existing baseline pain disorders may be more likely to be non-persistent with AI therapy. Future study should be conducted to determine if treatments for nocipastic pain improve AI persistence.

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